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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/054,313	10/22/2001	Stanley T. Crooke	ISPH-0613	5314

7590 05/18/2004

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EXAMINER	
SCHULTZ, JAMES	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 05/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/054,313	CROOKE ET AL.	
	Examiner	Art Unit	
	J. Douglas Schultz	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-45* is/are pending in the application.

4a) Of the above claim(s) *1-13 and 20-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-19 and 44* is/are rejected.

7)☒ Claim(s) *45* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Specification/Priority

The disclosure is objected to because of the following informalities: U.S. Application Number 09/684,254 has issued as U. S. Patent Number 6,376,661. This is not recited in the first paragraph of the specification. Appropriate correction is required.

Response to Election/Restrictions

Applicant's election of Group II with traverse in the papers filed November 10, 2003 and February 18, 2004 required in the restriction requirement in the paper filed October 9, 2003 is acknowledged. The traversal is on the ground(s) that each Group has a disclosed relationship to each other Group because the disclosed polypeptides share homology and Type 2 characteristics; applicants thus assert that the restriction based on the inventions being unrelated is improper. This is not found persuasive because this is not the proper test for whether inventions are related. Although applicant's contention that there is a disclosed relationship among the groups may be valid in the broadest sense of the term the term "related", this is not the definition set forth in MPEP § 806.04, MPEP § 808.01.

As per these sections, for inventions to be considered unrelated the inventions must not be disclosed as usable together, and must have a different mode of operation, different functions, or different effects. The fact that the disclosed polypeptides share homology and Type 2 characteristics does not speak to whether the Groups are disclosed as usable together, or whether they have different modes of operation, different functions, or different effects as set forth in the

restriction requirement. While each Group pertains to RNase H polypeptides in some way, only one Group is actually drawn to the polypeptide of RNase H itself. Thus, all claims where polypeptide homology might be considered a feature have been kept together; the remaining Groups are drawn to different molecules, such as antibodies, antisense molecules, or polynucleotides that encode RNase H, or different methods, and are not considered related because they have not been disclosed as useful together, and have different modes of operation, different functions, or different effects as outlined in the restriction requirement. Accordingly, these arguments are not considered convincing.

Applicants have noted that the methods of claims 24-26 utilize a polypeptide, not a polynucleotide as recited in the elected Group (II), and therefore do not properly belong in elected Group II. This is agreed with. Claims 24-26 are considered to be properly apart of Group I, which claims the polypeptide of RNase H, and are hereby withdrawn. The restriction requirement is still deemed proper and is therefore made FINAL.

This application contains claims 1-13, and 20-43 drawn to inventions nonelected with traverse in the papers filed November 10, 2003 and February 18, 2004. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14-19 and 44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The subject matter of the instantly claimed invention is drawn to a polynucleotide encoding a human RNase H, which may optionally be a type 2 human RNase H, and vectors and cells containing a human RNase H, and to a composition comprising a human RNase H and pharmaceutical diluents, or to a composition comprising type 2 human RNase H polynucleotide and antisense compounds.

At the outset it is noted that the rejected claims do not recite any sequence identifier. Said sequences are thus considered to be defined and claimed by their function (RNase H or its Type

2 subtype) rather than by any one specific structure. Accordingly such language embraces any sequence of any human RNase H, or in the case of claims 15, 19, and 44, any human type 2 RNase H, or any such molecule with analogous RNase H activity, known or yet to be discovered, along with any isoform or allele present within this species, or any variant that is within reasonable similarity from these families of proteins that retain RNase H or its type 2 function.

To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. Thus, an applicant complies with the written-description requirement by describing the invention, with all its claimed limitations, and by using such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical, structure/function correlation, methods of making the claimed product, and any combination thereof. The representative sample requirement may be satisfied by supplying structural or functional information, or a combination of both, such that one of skill in the art would be satisfied that applicants were in possession of the genus as claimed. Further, the size of the representative sample required is an inverse function of the unpredictability of the art.

The only human RNase H sequence taught in the specification is the Type 2 RNase H of SEQ ID NO: 1. While the specification refers to numerous RNase H isoforms from other species, the sequence of SEQ ID NO: 1 is the only support provided for *human* RNase H. In fact, the

specification at page 5, line 32 states that until this disclosure, no mammalian RNase H of any type had ever been disclosed. The presence of only one sequence of mammalian RNase H is not considered to meet the requirements for disclosure of a representative sample of structures that correlate to the genus of any molecule encompassing any human RNase H activity, or its type 2 subtype such that one of skill would consider applicants to be in possession of said genus. This is particularly true in view of A) the breadth of the human RNase H genus and its type 2 subtype (discussed below) and B) the lack of understanding of the specific structures that distinguish human RNase H function from non-human RNase H function. One of skill would not recognize from the specification that applicants were in possession of the instantly claimed human RNase H as opposed to other RNase H's that are non-human, because nothing in the specification provides any teaching by way of structure what it is that provides for human-specific vs. non-human specific activity.

There is a relatively substantial amount of data has been collected on various members of the RNase H family that suggests that the genera of RNase H and its type 2 subtype are extensive and diverse. However, there is little evidence that identifies structural commonalities that would arm one of skill in the art with the information necessary to understand how the genus of human RNase H differs from RNase H from another species. For example, the specification at the bottom of page 1 indicates that the RNase H family members possess various molecular weights, without discussing whether this is a reliable indicator of human vs. non-human RNase H. Page 4 addresses the diversity of the RNase H family by pointing to the lack of homology between E. coli RNase HI and HII, which is put at only 17%, which suggests that there is little structural similarity across RNase H family members, and renders the identification of species-specific

characteristics difficult at best. Applicants also note that no enzyme cloned from a species other than E. coli has displayed substantial homology to E. coli RNase HII. While the instant claims are drawn only to the family of human RNase H's or its type 2 isoforms, these teachings are considered to indicate that even within one species, the family of RNase H molecules is broad and diverse. It is maintained that nothing in the specification other than the one sequence of Type 2 RNase H (SEQ ID NO: 1) provides any teaching that unifies or otherwise informs one of skill what it is that confers human RNase H function, or the function of its Type 2 subtype.

One of skill in the art could not immediately envision the genus of human RNase H or Type 2 variants from the disclosure of only one human Type 2 sequence, particularly in the complete absence of any teaching by way of structure what it is that actually confers the functions of being A) human, or B) capable of carrying out Type 2 RNA/DNA hybrid hydrolysis (i.e. RNase H function). The genus is not immediately envisioned because the genus of any human RNase H and Type 2 variants is large, as pointed out above, and the genus is variable and the properties defining its "human" characteristics are poorly described or non-existent. One sequence is not considered to provide adequate support for a genus of RNase H that is both large and varied. Neither applicants specification nor the prior art actually disclose any correlation between the structure of RNase H, and the claimed functions inherent in a human transcript. Put simply, one of skill in the art would be unable to discern from either applicants specification or the prior art what it is that makes the transcripts human. Thus, because the distinguishing characteristics of the claimed genus are not described, claims to using the genus essentially amount to an invitation to experimentation to find human RNase H sequences, because one of

skill in the art would not be apprised as what structural features of RNase H provide for its human characteristics.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 14-19 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 6,001,653. Although the conflicting claims are not identical, they are not patentably distinct from each other.

The instantly claimed subject matter is drawn to polynucleotides encoding a human RNase H, which may optionally be a type 2 human RNase H, and vectors and cells containing same, and to compositions comprising same and pharmaceutical diluents or antisense compounds thereof, encompasses patented claims 1-5, drawn to a polynucleotide encoding a type 2 human RNase H, and vectors and cells containing same, and to compositions comprising same with antisense compounds.

Allowable Subject Matter

Claim 45 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. The prior art does not teach or fairly suggest methods of making purified human RNase H of SEQ ID NO: 1 comprising culturing cells transfected with a vector containing SEQ ID NO: 1 and expressing SEQ ID NO: 1, whereupon the RNase H is collected.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Douglas Schultz whose telephone number is 571-272-0763. The examiner can normally be reached on 8:00-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

James Douglas Schultz, PhD

SEAN McGARRY
PRIMARY EXAMINER
16 35